Knowledge Acquisition Session Report
NCI – DCP Protocol Information Office

KA Session Date: 4/25/00 **Time:** 2:00 p.m. – 4:00 p.m.

Session Topic: PIO Information Processes and Procedures

Knowledge Analysts: Lisa Chatterjee, Ram Chilukuri, Hilliard Hicks, Padma Behta, Oracle; Bill McCurry, Robert Harding, ScenPro, Inc.

Organization: Protocol Information Office, NCI Division of Cancer Prevention

Session Location: Rockville, Maryland

Type of Session:

_____ Interview _____ Task Analysis _____ Scenario Analysis
_____ Concept Analysis _____ Observation **X** Structured Interview
_____ Other:

Documentation: KA Session Report, CTEP-ESYS System Attributes Report

General Topic Area

Division of Cancer Prevention – Protocol Information Office: Information Processes and Procedures.

Session Goal

To elicit information related to DCP-PIO processes, system requirements, and existing data sources.

Report Summary

This report focuses on the process of administering DCP (Division of Cancer Prevention) research studies and on requirements for a system to support that process. The PIO (Protocol Information Office) named this system *Protocol Information Management System* (PIMS). PIO personnel asked that several system requirements be changed to "Must Have" status. NCI and research institutions sometimes have trouble determining which studies should go to DCP and which should go to the Cancer Therapy Evaluation Program (CTEP). DCP and CTEP plan discussions to clarify guidelines for those decisions. PIO personnel prepare CCOP protocol review packets, and they convene and schedule CCOP study review boards. PIO has less involvement in Contract study reviews. The PIO can access CCOP tracking data more easily than Contract tracking data. The PIO sometimes forwards protocols to CCS, but needs to clarify the criteria for doing so. CCOP studies may close in a variety of ways, but Contract studies close in a much more structured manner.

System Name and Storage

Protocol Information Office (PIO) personnel have named the new information system *Protocol Information Management System* (PIMS). NCI Office of Informatics servers will house the new system.

Major Steps to a DCP Study

PIO personnel provided feedback on the model of major steps common to all Division of Cancer Prevention (DCP) studies. Figure 1 shows this model with the beginning points and end points that separate each step.

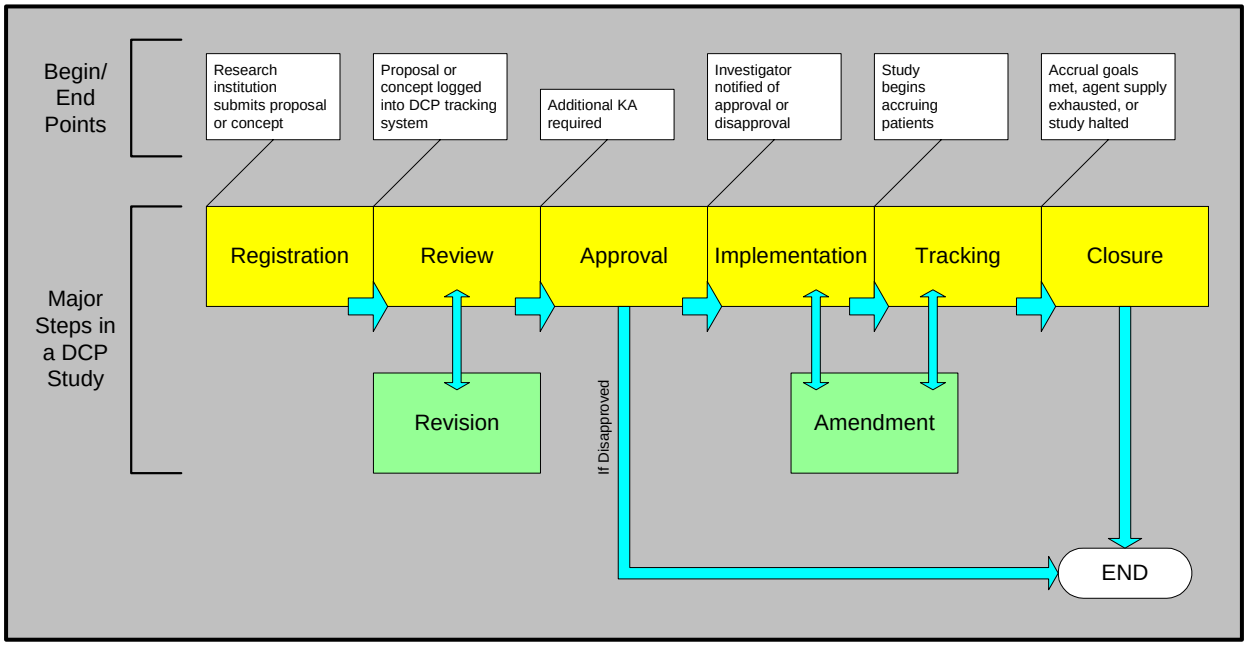

Figure 1: Major Steps of a DCP Study

PIO personnel verified that this model describes the DCP research study process at a high level. The sections that follow contain additional detail about each step. The details include changes to PIO's system requirements.

Registration

Division of Cancer Prevention (DCP) studies begin with registration of a document submitted by a research institution. Once a study concept or proposal and its details are logged into a DCP tracking system, the Registration step ends. Figure 2 shows the Registration step and its end points.

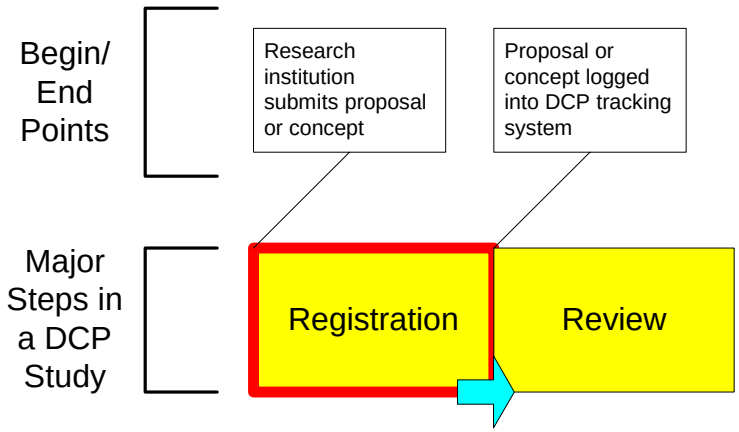

Figure 2: The Registration Step and its End Points

Differences in the Registration steps for Contract studies and Community Clinical Oncology Program (CCOP) studies are detailed below.

Contract Studies Registration

DCP sends Requests for Proposal (RFPs) to Master Agreement Holders (MAH). These cancer research institutions then submit proposals to DCP. A proposal includes a protocol that fully describes how a study will be conducted. The National Cancer Institute (NCI) has clearly defined the guidelines for the initiation of contract studies.

CCOP Studies Registration – As Is

DCP does not solicit research institutions to conduct CCOP studies. CCOP research bases instead submit concepts to NCI for CCOP studies. A concept briefly describes the plans for a study, and it is much shorter than a contract proposal.

CCOP research bases may submit concepts to DCP, to the Cancer Therapy Evaluation Program (CTEP), or to both. DCP manages cancer control and prevention studies. CTEP manages cancer treatment studies. A concept's cover letter explains why the study should be considered either a cancer control/prevention study or a cancer treatment study.

NCI personnel determine whether a study will be managed by DCP or by CTEP. CTEP personnel examine concepts and sometimes determine that they should be managed by DCP. DCP personnel sometimes receive concepts that they then pass on to CTEP.

CTEP and DCP personnel examine primary study endpoints to determine whether a study involves cancer control/prevention or cancer treatment. The table below shows the primary endpoints.

DCP Cancer Control/Prevention Study	CTEP Cancer Treatment Study
Primary Endpoints	Primary Endpoints
• Prevent the occurrence of cancer • Decrease complications • Improve a patient's quality of life • Recurrence of cancer	• Prolong a patient's life • Patient survival • Recurrence of cancer

CTEP and DCP personnel sometimes have difficulty determining where a study should be managed. The issues most likely to cause ambiguity are cancer recurrence and agent expertise.

- Cancer Recurrence

  Some studies examine methods to prevent or reduce the recurrence of cancer. For example, children who receive radiation therapy for cancer are more likely to develop other types of cancer later in life. NCI refers to recurrence prevention outcomes as secondary endpoints. Studies with secondary endpoints contain elements of both cancer treatment and cancer control/prevention. CTEP and DCP personnel plan discussions to resolve questions about where these studies should be managed.

- Agent Expertise

  CCOP research base personnel may believe that CTEP has more expertise than DCP with the agent to be used in a study. If research base personnel want CTEP to manage the study, they may write the cover letter so that the study appears to involve cancer treatment rather than cancer control/prevention. This can cause confusion and misclassification when NCI personnel determine who should manage the study.

<u>CCOP Studies Registration – To Be</u>

PIO personnel would prefer to receive cancer control/prevention concepts directly from the CCOP research bases. PIO plans to create a checklist to help research base personnel determine whether to send a concept to DCP or to CTEP.

Review, Revision, and Approval

The Review, Revision and Approval steps begin after a study is registered. The Approval step ends when the investigator is notified of protocol approval or disapproval. Multiple revisions may be required during the review process. Figure 3 shows the Review, Revision, and Approval steps with their end points. Additional KA is needed to clarify the end point between Review and Approval.

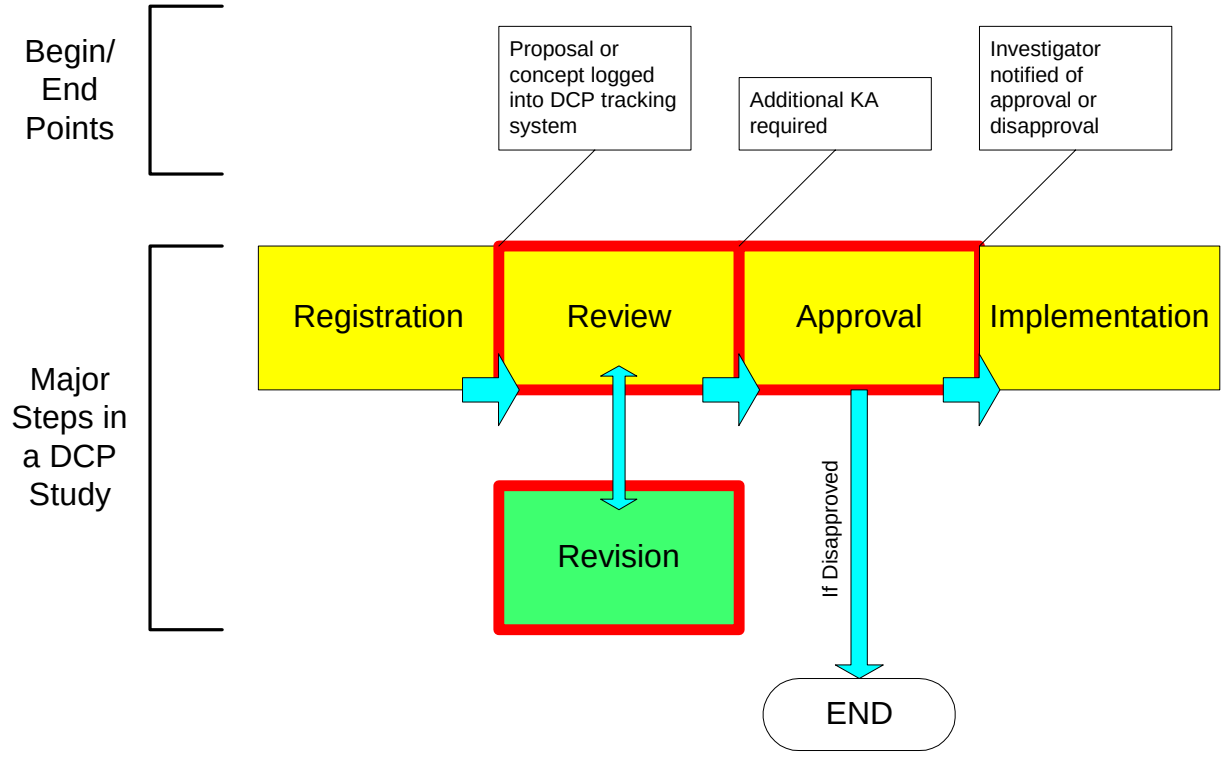

Figure 3: The Review, Revision and Approval Steps and their End Points

Contract studies demand less involvement from the PIO than do Community Clinical Oncology Program (CCOP) studies. Differences between the two types of studies are detailed below.

Contract Studies Review, Revision, and Approval

Contract proposals contain protocols that describe in detail how a study will be conducted. The DCP Technical Evaluation Panel (TEP) reviews the proposals and may recommend changes. If so, the Master Agreement Holders (MAH) must submit revised proposals within thirty days. The TEP reviews all competing proposals and awards the contract.

The DCP PIO has little involvement in this process beyond scheduling the TEP reviews. The DCP Contract Officer serves as a liaison between the MAH and the TEP. Figure 4 shows how PIO and the Contract Officer are involved in the Contracts Review, Revision and Approval steps.

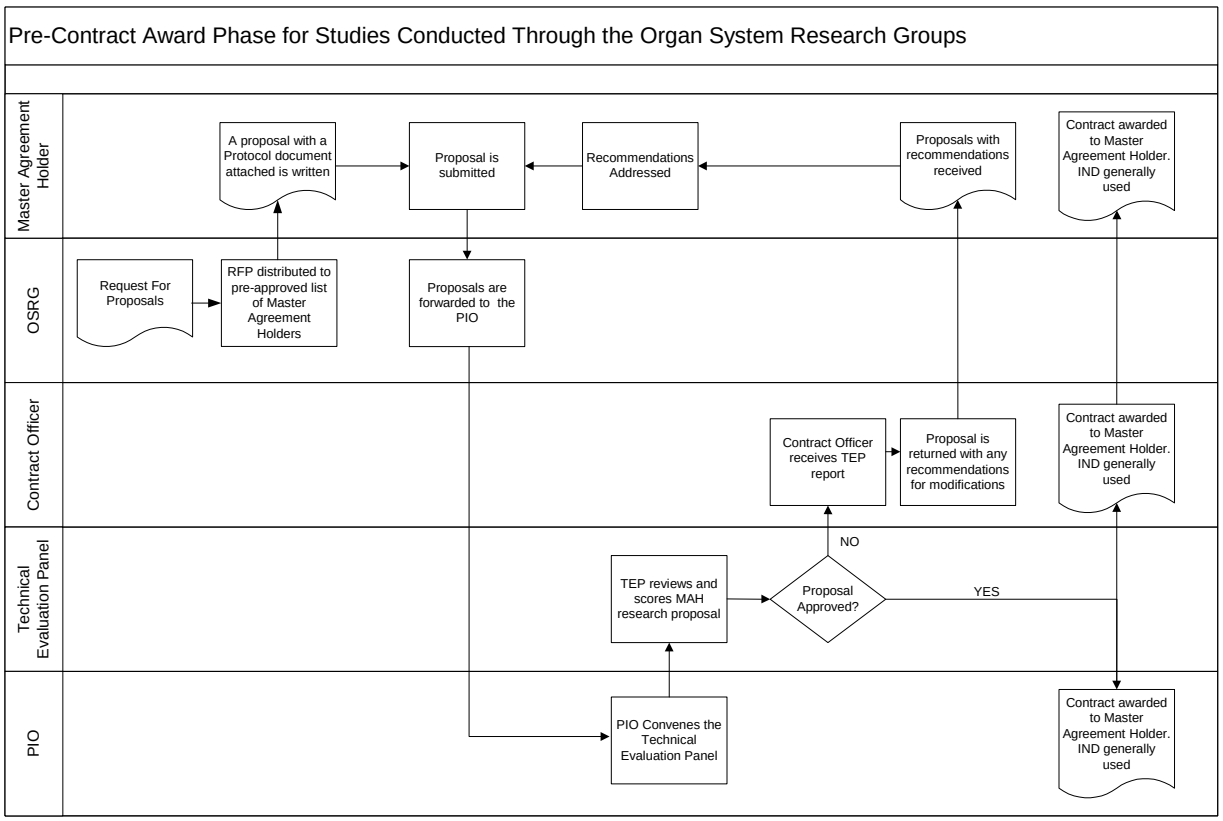

Figure 4: Registration, Review, Revision and Approval Steps for Contract Studies

The PIO assumes greater responsibilities in the Contract studies process after approval is granted and contracts are awarded.

CCOP Studies Review, Revision and Approval

PIO personnel convene Concept Review Committee (CRC) to evaluate concepts. This may require finding reviewers with special expertise from outside DCP. The CRC may approve a concept, disapprove a concept, or approve a concept with changes.

Once the concept is approved, the CCOP research base may submit a protocol. At that point, PIO personnel will prepare a protocol review packet and convene the Protocol Review Committee (PRC). The PRC consists of the same individuals as the CRC for any given study, but it has a different chairperson.

The PRC may approve the protocol, disapprove the protocol, or request changes to the protocol. The PRC chairperson communicates the results to the investigator who submitted the protocol. A change request may result in one or more rounds of revisions to the protocol. In many cases, PIO personnel must re-convene the PRC to evaluate the revisions.

PIMS System Requirements for Review, Revision and Approval

PIO personnel will evaluate CTEP's protocol review checklists to determine their value in preparing protocol review packets. PIO may adopt a version of the CTEP checklists for use in PIMS.

A database containing reviewer information would assist PIO in convening Concept and Protocol Review Committees. PIO feels that this item should be reprioritized to the "Must Have" category on the PIMS system requirements list.

Implementation

The Implementation step begins after protocol approval notification is delivered and is completed once institutions begin accruing patients. Figure 5 shows the Implementation step and its end points.

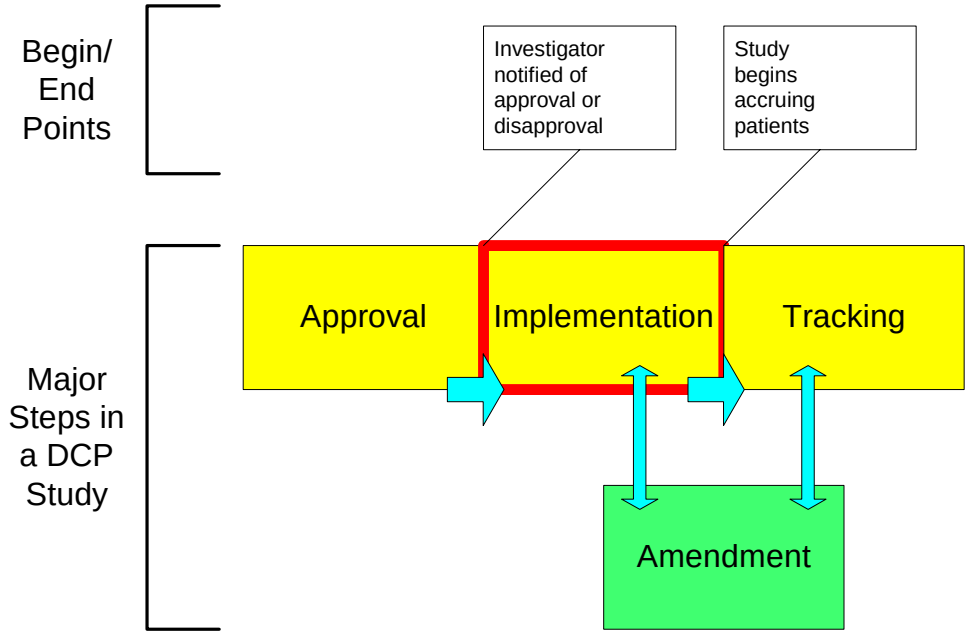

Figure 5: The Implementation Step and its End Points

Protocol Information Office (PIO) personnel confirmed that Implementation is a distinct step in the process and should be part of the model. They will provide additional detail on Implementation in a later KA session.

Some protocols accompany Investigational New Drug applications and must be sent to the Food and Drug Administration (FDA) before accrual can begin. Clinical Chemoprevention Study Associates (CCS) prepares the FDA document packet and sends it to the FDA. CCS also sends a copy of the packet to PIO. The packet includes:

- the IND sheet for each protocol
- a record of when the protocol was sent
- the protocol version identification
- a copy of the protocol version itself

Tracking

Tracking begins once the study begins accruing patients, and it continues until the study closes. Figure 6 shows the Tracking step and its end points.

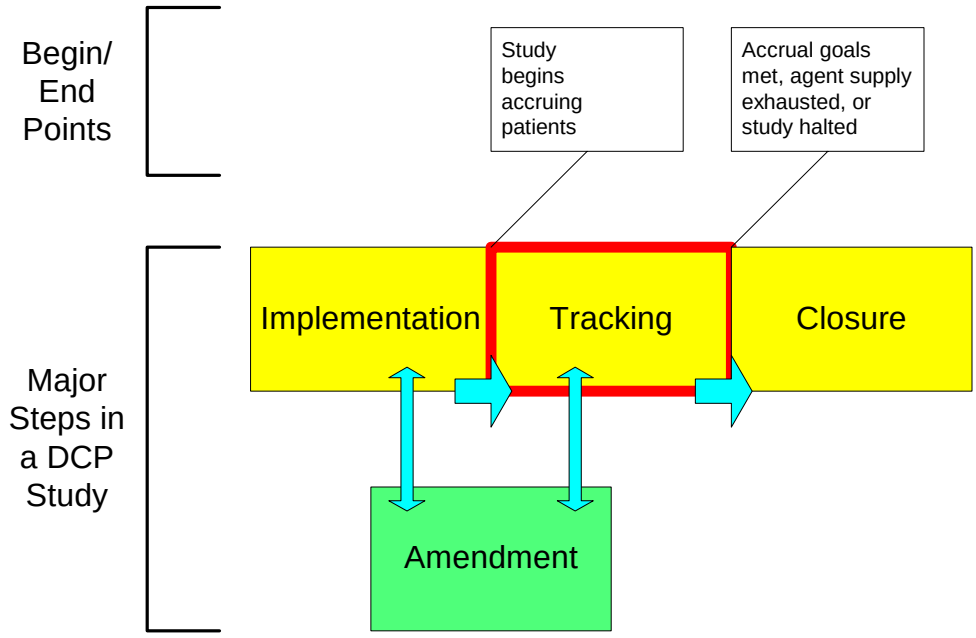

Figure 6: The Tracking Step and its End Points

The Protocol Information Office (PIO) personnel frequently respond to questions about research study progress. Effective study tracking greatly assists the PIO in answering these questions.

Contract Studies Tracking

Master Agreement Holders (MAH) must forward quarterly patient accrual reports to the DCP contract officers and project officers. The project officers then forward those reports to CCS, and CCS enters the accrual information into its database. Figure 7 shows the Contract study accrual reporting process.

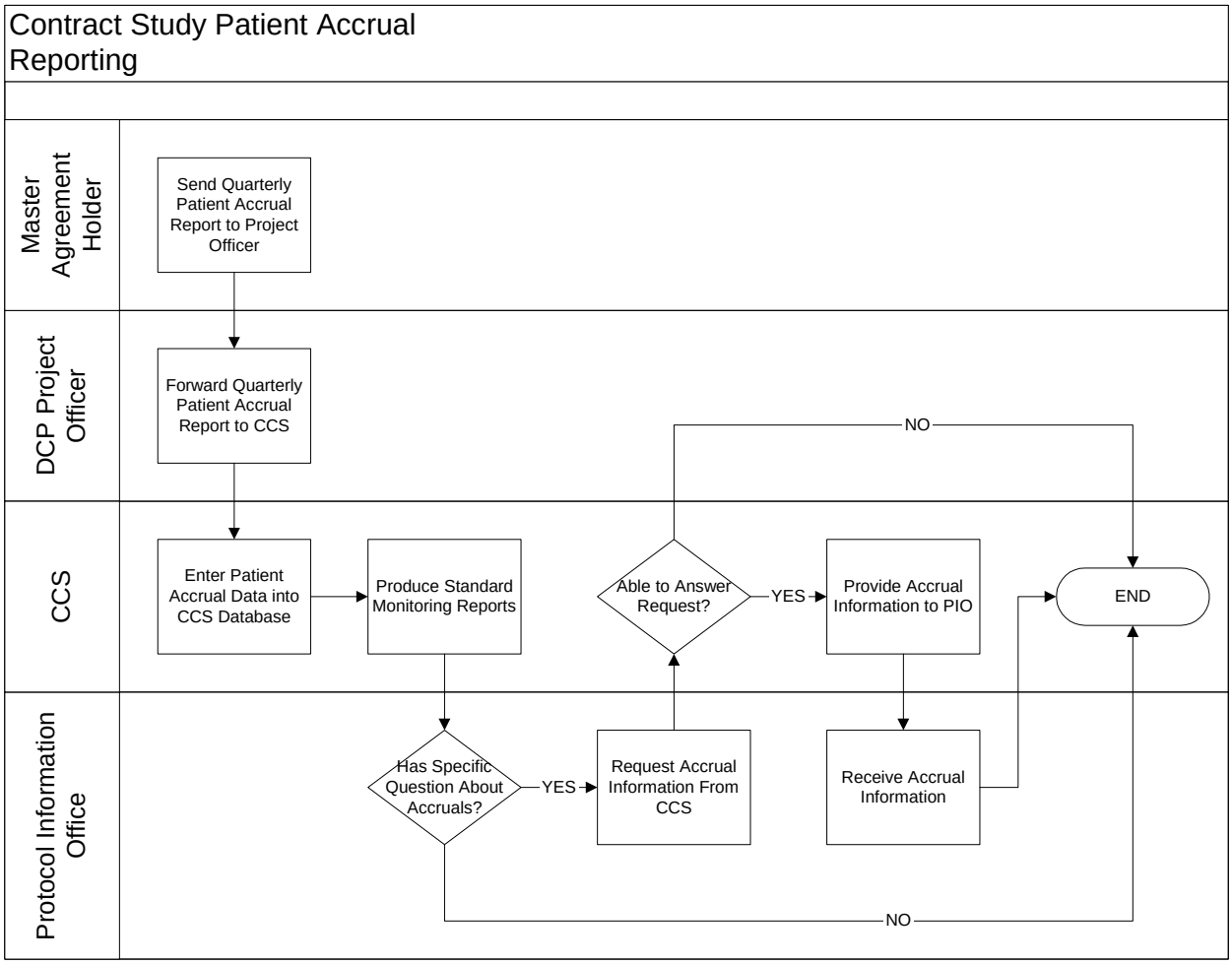

Figure 7: Contract Study Patient Accrual Reporting Process

PIO personnel cannot access the CCS database directly. CCS has not always been able to respond effectively to PIO inquires about studies in progress. PIO personnel expressed the need to know which CCS employee is working with any given protocol.

CCOP Studies Tracking

PIO personnel can access most CCOP patient accrual information when they want. Figure 8 depicts CCOP Study Patient Accrual Reporting.

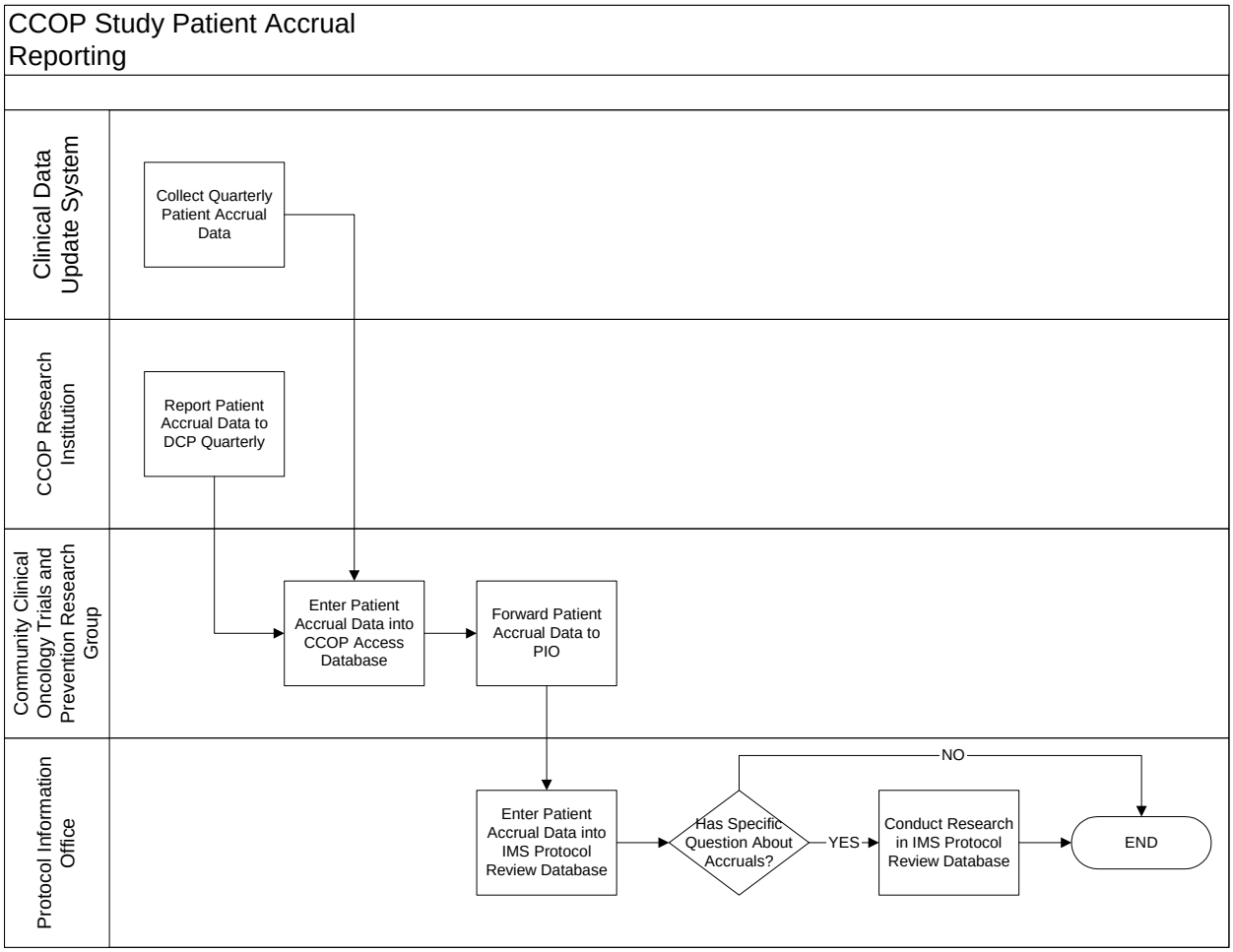

Figure 8: CCOP Study Patient Accrual Reporting

The Clinical Data Update System (CDUS) collects and stores patient accrual data for CCOP studies back to March 5, 1998. CCOP research institutions report quarterly patient accrual information to the DCP Community Clinical Oncology and Prevention Trials Research Group. A program analyst in that group enters the accrual information into the CCOP Access Database. She then forwards the accrual information to PIO. PIO personnel enter the patient accrual information into the Protocol Review Database.

PIMS System Requirements for Tracking

After reviewing the MoSCoW list from the April 11 KA session, PIO personnel felt that several items needed clarification or reprioritization.

- Target Codes

Target codes should include organ site, symptom, and population sub-group codes in addition to disease codes. DCP studies may involve only one or two of these factors, which complicates tracking and reporting. PIO personnel will ask Frank Hartel in the NCI Office of Informatics for assistance in developing effective codes.

- Numbering System

PIO personnel confirmed that a consistent numbering system for studies and study documents is a "Must Have" item. This will promote more effective study tracking and reporting.

- Tracking Each Step of the Process

PIO personnel confirmed that tracking each step of the protocol review and administration process is a "Must Have" item.

- Standard Queries

PIO personnel felt that standard queries for tracking dates should be reprioritized to a "Must Have" item. This includes queries for tracking elapsed time between steps and queries for tracking progress against timelines.

- Allow Users to See Where Protocol Is in Process

One of the system requirements was to allow users (internal and external) to see where a protocol stands in the approval process. PIO personnel felt that this feature should be reprioritized to "Must Have".

- Tickler System

PIO personnel felt the tickler system should be moved to the "Must Have" category. This system would allow PIO personnel to run reports on items that are due for completion or action.

Amendment

Investigators sometimes request that protocols be changed after approval. These changes are called amendments. Amendments may occur any time during Implementation or Tracking steps. The Division of Cancer Prevention (DCP) must approve any amendment to a DCP protocol. Figure 9 shows the Amendment step in relation to the Implementation and Tracking steps.

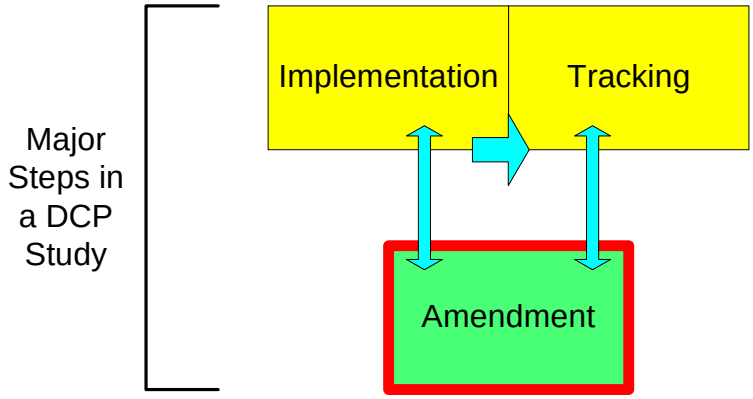

Figure 9: The Amendment Step

Investigators may request protocol amendments for the following reasons:

- change of target organ
- change of drug type
- change of eligibility criteria
- patient name or address change

PIO personnel will provide more detail about amendments in a future KA session.

Closure

Division of Cancer Prevention (DCP) studies complete at some point after patients start accruing. Not all studies meet their patient accrual goals before completing. Figure 10 shows the Closure step and its beginning point.

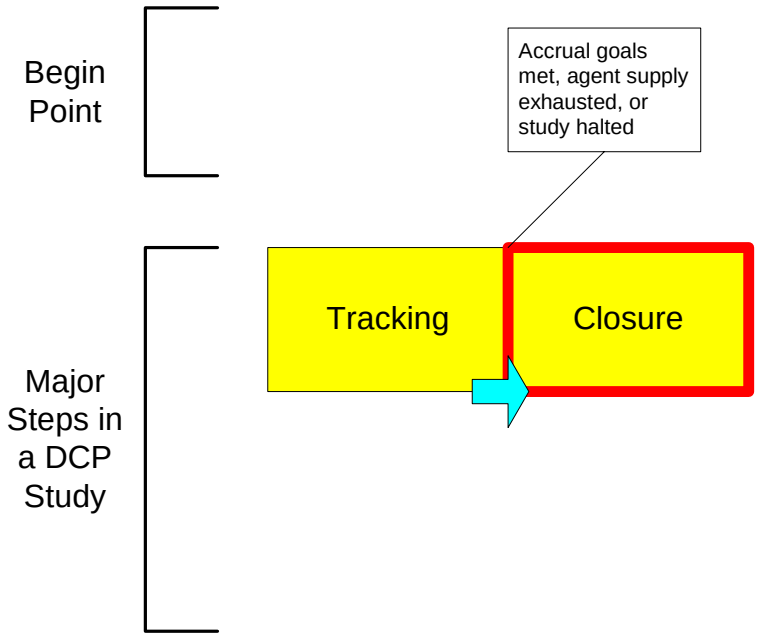

Figure 10: The Closure Step and its Beginning Point

Contract Studies Closure

Contracts define the completion criteria for Contract studies. However, DCP may close a Contract study if the medical monitor and the project officer agree that the study should be closed.

CCOP Studies Closure

Completion of CCOP studies is less structured than completion of Contract studies. A study may meet its patient accrual goals and subsequently close. The study may run out of agent supply, forcing it to close. The cooperative group may decide to close a study. The cooperative group is required to send notification of study completion to the PIO. Notification usually arrives via amendment, CDUS update, or phone call.

Forwarding Studies to CCS

Clinical Chemoprevention Study Associates (CCS) requires information about some protocols but is not concerned with other protocols. PIMS will require a mechanism to identify protocols that should be forwarded to CCS. Figure 11 shows the process of deciding whether to forward a protocol to CCS.

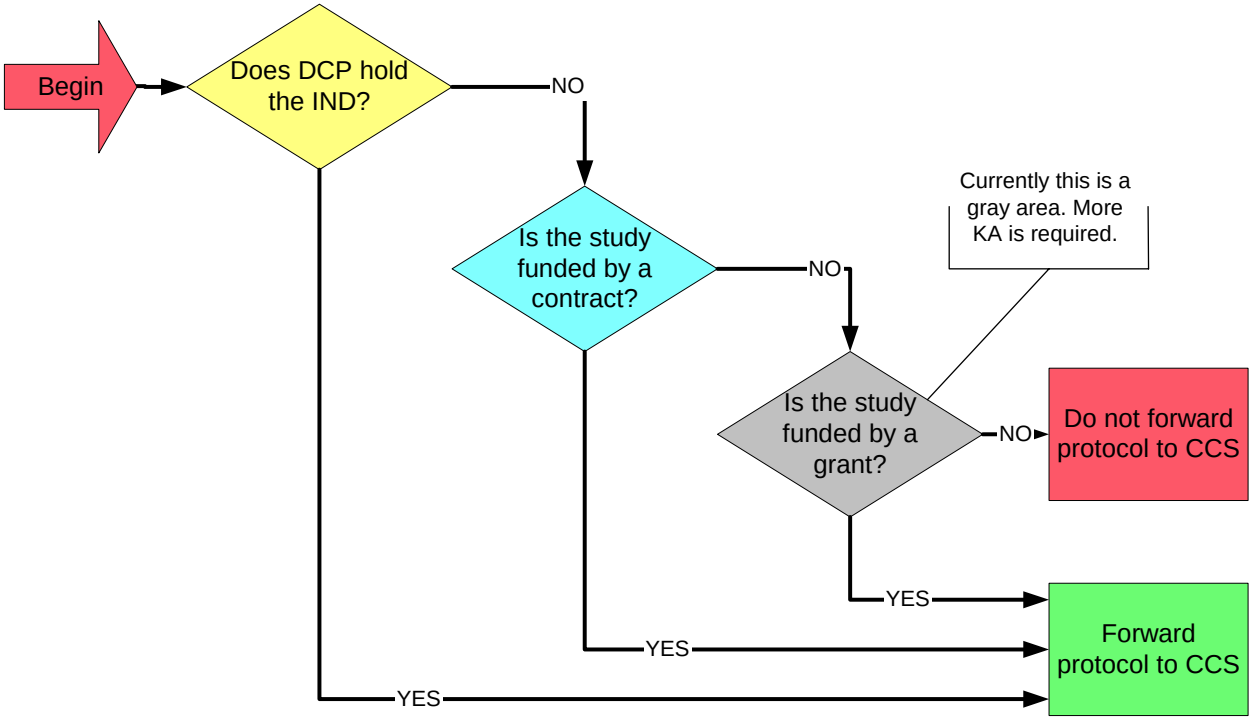

Figure 11: Decisions in Determining Whether to Forward a Protocol to CCS

CCS provides DCP with Investigational New Drug (IND) filing technical assistance. Any protocols related to INDs owned by DCP should go to CCS. CCS also provides monitoring for all Contract protocols, so contract protocols should be forwarded to them.

Grant-funded protocols will not normally be forwarded to CCS. Master Agreement Holders monitor their studies and report patient accrual data to DCP. However if the investigator or research institution requests monitoring assistance from DCP, CCS may provide that monitoring. Grant-funded protocols remain an area of uncertainty in this decision making process.

PIO personnel are not yet sure how they want this process to work in the future. They plan discussions to resolve these questions and will provide clarification in a later KA session.

Summary of System Requirement Clarifications

The table below summarizes the PIO's clarifications and changes to system requirements. The ID numbers correspond to the April 12 version of the MoSCoW list.

ID #	Description	Clarification
10	Target codes for creating abstracts based on • Organ type • Target symptoms • General symptoms • Population sub-groups PIO will confer with Frank Hartel 301 435 3869	Target codes are an addition to a system requirement already identified as "Must Have"
20	Consistent numbering system	PIO reiterated the need to keep this requirement a "Must Have"
40	Track each step of the concept/protocol review and administration process: • Scheduling reviews • Assigning reviewers • Capturing the review results	PIO reiterated the need to keep this requirement a "Must Have"
120	Standard queries for: • Tracking the lapsed time between each step of the process • Tracking progress against timelines	PIO identified these two query types as "Must Have"
140	Allow users (internal and external) to see where a protocol is in the approval process	PIO stated that this requirement is important enough to be a "Must Have"
160	Database of reviewer information	This requirement will aid the PIO in convening review boards and should be a "Must Have"
170	Tickler system to put timelines on required actions and to track progress against these timelines	PIO stated that this requirement is important enough to be a "Must Have"

PIO Research for Future KA Sessions

Protocol Information Office personnel identified a number of areas requiring further research on their part. These areas will be explored further in future KA sessions. The areas for further PIO research are:

- Determine the number of people who will use PIMS (both the total and concurrent number)
- Reflect on PIO interaction with CTEP and PDQ with input from Dr. Ford
- Determine terms to be used as codes (with input of Frank Hartel: 301 435 3869) for:
  - Target Organs
  - Symptoms
  - Sub-groups (population groups)
  - General symptoms
- Define the number of disease code levels with input of Frank Hartel
- Provide copies of an IND sheet and a FDA Packet
- PIO will work towards setting business rules to determine if a study will be forwarded to CCS
- Explore the commonalities and differences between CCOP and Contracts' Implementation of studies
- Explore the commonalities and differences between CCOP and Contracts' Amendments step
- Work on what parts of existing data sources, including historical data should be incorporated into PIMS
- Review the CTEP-ESYS Attribute Description Report focusing on domain values:
  - Will we need these attributes or values?
  - Do we do this?
  - Do we refer to this attribute or value by another name?
  - Do we need something else?

Entries for Domain Dictionary

Agent Expert: Term coined by DCP contractor Clinical Chemoprevention Studies Associates. An agent expert is a CCSA employee who deals with agent related issues in contract studies through the DCP.

Contract Officer: Liaison between Master Agreement Holders and The DCP regarding legal matters relating to contract studies.

Endpoint: A primary or secondary outcome variable used to judge the effectiveness of a treatment in a clinical trial. A primary endpoint might be the survival of the patient. The secondary endpoint could aim for the prevention of cancer recurrence.

Medical Monitor: DCP doctor who performs a function similar to a Disease Monitor in the CTEP process. Deals with contract studies. Additional KA needed.